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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,122	09/11/2006	**Brenda M. Ogle**	07039-463US1	4639

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,122	OGLE ET AL.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *9,10,12 and 16-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-17, species A, D and F) in the reply filed on May 15, 2008 is acknowledged.

2. Claims 9, 10, 12 and 16-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species and inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 15, 2008.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

4. Claims 1-8, 11 and 13-15 will be examined.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on November 27, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Interpretation

6. Applicants did not define the term "random nucleic acid molecules", therefore it is considered as any nucleic acid molecules.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 6 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. (PNAS USA, vol. 95, pp. 14447-14452, 1998; cited in the IDS).

Regarding claim 1, Wagner et al. teach a method for determining lymphocyte diversity in a subject, said method comprising

a) providing labeled nucleic acid molecules from a population of said subject's lymphocytes, wherein each said labeled nucleic acid molecule encodes a lymphocyte receptor or a portion thereof (page 14447, fourth paragraph; page 14448, second and third paragraph);

b) hybridizing said labeled nucleic acid molecules or fragments of said labeled nucleic acid molecules with a population of random nucleic acid molecules (page 14448, second and third paragraph, where the random nucleic acid molecules are the probes spanning the N-D-N region); and

c) determining lymphocyte diversity of said subject by assessing hybridization of said labeled nucleic acid molecules with said population of random nucleic acid molecules (page 14448, third and fourth paragraphs; Fig. 1; Fig. 2).

Regarding claims 2 and 3, Wagner et al. teach the probes attached to microtiter plates (page 14448, third paragraph).

Regarding claim 6, Wagner et al. teach the probes attached to microtiter plates, therefore they inherently teach a plurality of different regions with different random nucleic acid mmolecules (page 14448, fourth paragraph).

Regarding claims 13-15, Wagner et al. teach T-cell receptor β chain sequences (Abstract; page 14448, second paragraph).

9. Claims 1-3, 6 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al. (Immunogenetics, vol. 52, pp. 35-45, 2000).

Regarding claim 1, Yoshida et al. teach a method for determining lymphocyte diversity in a subject, said method comprising

a) providing labeled nucleic acid molecules from a population of said subject's lymphocytes, wherein each said labeled nucleic acid molecule encodes a lymphocyte receptor or a portion thereof (page 36, fifth, sixth and seventh paragraph; page 37, first and second paragraph);

b) hybridizing said labeled nucleic acid molecules or fragments of said labeled nucleic acid molecules with a population of random nucleic acid molecules (page 37, third and fourth paragraph, where the random nucleic acid molecules are the probes listed in Table 2 on page 38); and

c) determining lymphocyte diversity of said subject by assessing hybridization of said labeled nucleic acid molecules with said population of random nucleic acid molecules (page 37, fourth paragraph; Fig. 3; Fig. 4; Table 1).

Regarding claims 2 and 3, Yoshida et al. teach the probes attached to microtiter plates (page 37, third paragraph).

Regarding claim 6, Yoshida et al. teach the probes attached to microtiter plates, therefore they inherently teach a plurality of different regions with different random nucleic acid molecules (page 37, third paragraph).

Regarding claims 13-15, Yoshida et al. teach T-cell receptor β chain sequences (Abstract; Table 2).

10. Claims 1-3, 6, 7 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Lebed et al. (J. Biomol. Struct. Dynam., vol. 18, pp. 813-823, 2001).

Regarding claim 1, Lebed et al. teach a method for determining lymphocyte diversity in a subject, said method comprising

a) providing labeled nucleic acid molecules from a population of said subject's lymphocytes, wherein each said labeled nucleic acid molecule encodes a lymphocyte receptor or a portion thereof (page 814, paragraphs 4-6; page 815, first paragraph; page 818, paragraphs 3-5);

b) hybridizing said labeled nucleic acid molecules or fragments of said labeled nucleic acid molecules with a population of random nucleic acid molecules (page 814, second paragraph; page 815, second and third paragraph; page 818, last paragraph); and

c) determining lymphocyte diversity of said subject by assessing hybridization of said labeled nucleic acid molecules with said population of random nucleic acid molecules (page 819; page 820; page 821; Table 1).

Regarding claims 2 and 3, Lebed et al. teach the probes attached to a chip (page 814, second paragraph).

Regarding claim 6, Lebed et al. teach the probes attached to chip, therefore they inherently teach a plurality of different regions with different random nucleic acid molecules (814, second paragraph).

Regarding claim 7, Lebed et al. teach fluorescent labels (page 815, first paragraph).

Regarding claims 13-15, Lebed et al. teach T-cell receptor β chain sequences (Abstract; page 814, paragraphs 4-6).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

> subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 4, 5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. (PNAS USA, vol. 95, pp. 14447-14452, 1998; cited in the IDS) and Fulton et al. (Clin. Chem., vol. 43, pp. 1749-1756, 1997).

A) The teachings of Wagner et al. are presented above. They teach solid support being a multiwell plate, but do not teach beads, fluorescent labels or flow cytometry.

B) Fulton et al. teach multiplexing of analyte detection reaction using flow cytometry with fluorescently-labeled beads (Abstract; page 1749, second paragraph).

Regarding claim 4, Fulton et al. teach oligonucleotide probes immobilized on microspheres (page 1751, third seventh paragraph).

Regarding claim 5, Fulton et al. teach detection of nucleic acid hybridization by flow cytometry (page 1752, third paragraph).

Regarding claims 7 and 8, Fulton et al. teach labeling of target nucleic acids with fluorescent dyes FITC and bodipy (page 1750, third paragraph; page 1751, last paragraph; page 1752, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used probes immobilized on beads and flow cytometry of Fulton et al. in the detection of lymphocyte diversity of Wagner et al. The motivation to do is provided by Fulton et al. (page 1755, second and last paragraphs):

"These studies have demonstrated the ability of the FlowMetrix system to perform highly multiplexed assays for analysis of specific protein–protein interactions, such as immunoassays, and for analysis of specific DNA sequences. The system provides several advantages for analysis of

biologically and medically relevant molecules, including speed, economy, and advanced analytical capabilities. The system reduces assay time by performing multiple analyses simultaneously rather than sequentially. The no-wash format of many microsphere-based assays, particularly in the final detection step, is considerably faster than microtiter-based assays that require multiple washing steps to remove excess reagents. In addition, the rapid kinetics of microsphere-based assays allow shorter incubation times than conventional solid phase assays. The reduced assay time also reduces labor costs for performing multiple analyses. Reagent usage for microsphere-based assays is 10- to 1000-fold less than microtiter-based assays. Multiplexing allows unique analysis of molecular interactions that can only be performed in a multiplexed format. "

The FlowMetrix system represents a revolutionary new technology that can be applied to virtually any application that requires analysis of molecular interactions, including basic research, clinical diagnostic testing, highthroughput drug screening, environmental testing, and agricultural testing. This system is unique in its ability to provide multiplexed, high-throughput analysis coupled with real-time data analysis. The system offers excellent sensitivity, precision, speed, and economy."

13. Claims 4, 5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al. (Immunogenetics, vol. 52, pp. 35-45, 2000) and Fulton et al. (Clin. Chem., vol. 43, pp. 1749-1756, 1997).

A) The teachings of Yoshida et al. are presented above. They teach solid support being a multiwell plate, but do not teach beads, fluorescent labels or flow cytometry.

B) Fulton et al. teach multiplexing of analyte detection reaction using flow cytometry with fluorescently-labeled beads (Abstract; page 1749, second paragraph).

Regarding claim 4, Fulton et al. teach oligonucleotide probes immobilized on microspheres (page 1751, third seventh paragraph).

Regarding claim 5, Fulton et al. teach detection of nucleic acid hybridization by flow cytometry (page 1752, third paragraph).

Regarding claims 7 and 8, Fulton et al. teach labeling of target nucleic acids with fluorescent dyes FITC and bodipy (page 1750, third paragraph; page 1751, last paragraph; page 1752, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used probes immobilized on beads and flow cytometry of Fulton et al. in the detection of lymphocyte diversity of Yoshida et al. The motivation to do is provided by Fulton et al. (page 1755, second and last paragraphs):

"These studies have demonstrated the ability of the FlowMetrix system to perform highly multiplexed assays for analysis of specific protein–protein interactions, such as immunoassays, and for analysis of specific DNA sequences. The system provides several advantages for analysis of biologically and medically relevant molecules, including speed, economy, and advanced analytical capabilities. The system reduces assay time by performing multiple analyses simultaneously rather than sequentially. The no-wash format of many microsphere-based assays, particularly in the final detection step, is considerably faster than microtiter-based assays that require multiple washing steps to remove excess reagents. In addition, the rapid kinetics of microsphere-based assays allow shorter incubation times than conventional solid phase assays. The reduced assay time also reduces labor costs for performing multiple analyses. Reagent usage for microsphere-based assays is 10- to 1000-fold less than microtiter-based assays. Multiplexing allows unique analysis of molecular interactions that can only be performed in a multiplexed format. "

The FlowMetrix system represents a revolutionary new technology that can be applied to virtually any application that requires analysis of molecular interactions, including basic research, clinical diagnostic testing, highthroughput drug screening, environmental testing, and agricultural testing. This system is unique in its ability to provide multiplexed, high-throughput analysis coupled with real-time data analysis. The system offers excellent sensitivity, precision, speed, and economy."

14. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lebed et al. (J. Biomol. Struct. Dynam., vol. 18, pp. 813-823, 2001) as evidenced by Allen et al. (U.S. Patent No. 6,017,710 A).

A) Lebed et al. teach Texas Red as a fluorescent label (page 815, first paragraph), but do not teach any of the labels listed in claim 8.

B) As evidenced by Allen et al., Texas Red is one of many fluorescent labels, including FITC, phycoerythrin or allophycocyanin (col. 14, lines 3-11).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used alternative fluorescent labels of Allen et al. in the method of Lebed et al., since they are functionally equivalent compounds. As stated in MPEP 2144.06:

2144.06 Art Recognized Equivalence for the Same Purpose

>II. < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); ** *Smith v. Hayashi*, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium

were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.).

An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

15. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lebed et al. (J. Biomol. Struct. Dynam., vol. 18, pp. 813-823, 2001) and Wang et al. (Nature Biotechnol., vol. 18, pp. 457-459, 2000).

A) Lebed et al. teach labeled DNA molecules (page 815, first paragraph), but do not teach labeled RNA molecules.

B) Wang et al. teach hybridization of labeled RNA molecules to DNA chips (page 457; page 459, first and second paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used labeled RNA molecules of Wang et al. in the method of Lebed et al. The motivation to do so, provided by Wang et al., would have been that using RNA molecules permitted detection of low-abundance mRNAs and clinical samples (Abstract; page 458, fourth paragraph).

16. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

/Teresa E Strzelecka/
Primary Examiner, Art Unit 1637
July 15, 2008